CURRENT CONCEPTS OF PROPHYLAXIS*

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PROPHYLAXIS as an element of venereal disease control has a long and fascinating history and dates from the 16th century, when Fallopius wrote of the use of a linen sheath for protection. In the 17th century Mme. de Sevigné wrote of the use of goldbeater's skin (animal caecum). The rapid advances in prophylactic methodology and practice, beginning with the experience of Credé in using 1% silver nitrate in 1872, followed by discoveries in pharmacologic and related industrial technology in union with medical research, were important factors in the control of ophthalmia neonatorum through prophylaxis and in related action in the prevention of genital infections. Gonorrhea and syphilis were well known for their consequences; their seriousness was appreciated. They were feared, to some extent, by those at risk. Further, the results of the diseases in terms of social and economic costs were well understood. The baby blinded by gonorrheal ophthalmia neonatorum or infected with congenital syphilis raised the level of social and political concern to the point of action in terms of requiring, by law, prophylactic treatment of the eyes of all neonates. In due time serologic testing (and treatment, if needed) was required in the United States before a marriage license could be issued. While this law does not preclude premarital contact or out-of-wedlock births, the effect in reduction of congenital syphilis over the years has been dramatic. In similar fashion, the high rates of absence from duty and hospitalization resulting from venereal disease (VD) in the military services led to the development of highly effective, well-planned, and well-

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implemented programs for the control of VD in which prophylactic practices played an important role.

Parenthetically, I might note that one of the reasons for discontinuing the long-term prophylactic studies of the Venereal Disease Research Laboratory (VDRL) of the U.S. Public Health Service at Staten Island, N.Y., the leading center for prophylactic studies in the United States, in 1950 was the cessation of interest in prophylaxis in the armed services. The rationale was that "it was cheaper to treat the disease than to try to prevent it."[1]

In light of the present continued rise in VD throughout the world, including the United States, which began in 1957, and with the associated increasing social and economic costs of this epidemic, it would seem appropriate to consider once again the possible contribution that prophylaxis might make in stemming the rise. In this paper the type of prophylaxis to be discussed consists of methods which are self-administered and do not require a prescription, such as the condom and chemical agents which can be applied locally before or after coitus. The recent work by Darrow,[2] as well as findings reported in the Battelle Institute Report,[3] clearly point out some of the problems existing today—behavioral, motivational, and educational—with respect to the use of the condom. However, there is a growing effort to promote the use of this device throughout the world in family-planning programs. This movement, in association with the innovative approaches in marketing techniques such as the colored condom,[4] for example, all suggest that the successes of the population program may contain some lessons which have potential for incorporation into present VD control programs.

In prevention of the sexually transmissible diseases there are three types of prophylaxis; the first two depend primarily upon the patient, while the third requires medical intervention. The condom, originally perceived as a mechanical barrier to the transmission of VD is now, in most of the world, regarded more as a contraceptive. Local chemical applications to the vagina or the external genitalia for prophylactic purposes have a low level of usage at present. Antibiotics are widely used for treatment of the sexual contacts of patients (abortive therapy). In some countries prostitutes take antibiotics either as self-medication or under medical supervision to provide protection. The precoital visual inspection which many prostitutes practice affords further protection.

The development of modern prophylactic procedures for syphilis has

drawn much from experimentation with the rabbit from which, I believe, it is possible to predict the effectiveness in man with a high degree of certainty. For gonorrhea, with no animal model except the scarce and expensive chimpanzee, the developments have had to be based upon epidemiologic trials, field experience, and rare studies in human volunteers. A brief summary of this experience may be of interest. In my opinion, experience has demonstrated conclusively the value of prophylaxis for the male, But success is dependent upon a well-organized, large-scale approach which is carried out best under military conditions or in well-managed brothels. Frequent or constant failure of the individual to practice prophylactic behavior is well recognized and documented. The passionate and often unplanned nature of sexual relations, judgment often being additionally impaired by alcohol, works against self-protection or protection of one's partner—for prophylactic or contraceptive purposes—particularly when such measures are not unrelated to coitus. Further, when the patient presents herself at term and often in labor, without prior examination for gonorrhea or syphilis, the practice of prophylaxis offers the only feasible means of prevention of gonorrheal infection in the newborn. The value of 1% silver nitrate as prophylaxis for ophthalmia neonatorum was shown by Credé in 1872. This procedure has been responsible for the dramatic worldwide reduction of blindness, with resultant social benefits. Complacency resulting from the success of the method and a fear of possible local reaction has led to failure to practice silver-nitrate prophylaxis routinely in many hospitals. This has resulted in scattered outbreaks, which bring about renewed appreciation of the seriousness of the problems and thus the reinstatement of the procedures as routine.[5]

With the development of ocular prophylaxis by means of silver preparations came studies of the use of silver preparations for prophylaxis and therapy of genital gonorrhea, and the studies that led to the use of 33% calomel ointment as a prophylaxis for syphilis. The seriousness of the diseases and the lack of specific therapeutic agents fostered interest in and widespread acceptance of the use of prophylactic techniques. This was done to promote individual use by the concerned individual for self-protection, and to promote also the public-health approach, as is possible in the military. Under these conditions prophylactic stations could be set up and staffed to provide services to military personnel in a given high-risk area. The potential value of prophylactic stations—involving the local applica-

tion of 33% calomel ointment and urethral instillation of mild silver proteinate—was shown in World War I.[6] The classic St. Nazaire experience resulted in reduction of the rates for all venereal diseases from 625 per 1,000 per month to 110 in a period of three months through compulsory prophylaxis administered to all men returning from leave. In World War II improvements were made; the value of a single postexposure application for the male was demonstrated; and individual administration and prophylactic stations were promoted. Various formulations were studied in view of the need for a preparation that gave protection against both gonorrhea and syphilis and that could be packaged in a single tube and used immediately after exposure. In addition to these preparations, the condom was promoted and widely distributed, prophylactic stations were established as appropriate, and all methods were integrated into a comprehensive and well-administered control program. This recently has been summarized by Greenberg.[7]

The basic prophylactic agent still was calomel, in combination with a wide variety of other agents such as silver compounds, sulfonamide, and surfactants, the latter being of particular importance in enhancing the prophylactic properties of various agents as shown by Arnold's work at the VDRL.[3,4] The Sanitube, containing 30% calomel, oxyquinoline benzoate, tricresol, and hydroxyethylamin soap in a Benlarlan (Bachman) base was found highly effective when used properly; it is still marketed. I am told that more than half a million tubes are produced each year. This suggests the size of the potential population of males concerned with self-protection by local means—a population which might be enlarged greatly by appropriate educational and motivational programs.

The protection of the female by local, self-administered preparations has been of secondary concern for many reasons. The Edwards' study[8] of Progonasyl[9] has been criticized on epidemiologic grounds. However, Funes and Aguilar,[10] in a well-controlled study of governmentally regulated prostitutes, demonstrated that postcoital douching with an 0.1% Orvus-Mapharsen solution reduced the rate of infection in six professionally active women from 11 in six months to one in the next six months. Obviously, the effectiveness of any douche depends upon the composition of the preparation used as well as on the methods of use. Therefore, it is not scientifically valid to speak of douching per se as a technique, as usually is done in dismissing the procedure as valueless. In another study with prostitutes, Ohno and co-workers[11] found that a high degree of

protection was obtained through the use of vaginal foaming tablets containing penicillin, chloremphenicol, or oxytetracycline. The use of antibiotic and chemoprophylactic agents has been shown to be effective before or after contact.[12] Abortive or prophylactic treatment of the contact, an essential part of modern VD control programs, can be considered a method of prophylaxis. But this type of approach also is complicated by the problems of motivation and behavior, since the individual at risk must take medication as directed or report for injections. In addition, all preparations used require medical supervision and prescription. Finally, the well-known problems of drug reaction and the resistance of pathogens must be considered in decisions regarding circumstances under which these techniques should be used.

There is reason to believe that major factors involved in the worldwide increase in VD are the increased risks of contact with infected partners and the change in pattern of contraceptive practices. Casual sexual partners are found to come from more widespread geographical areas than previously because of the increasing mobility of populations and the tremendous increase in tourism.[13] Analyses of gonorrhea patterns in Sweden and England have suggested that the rise in rates may well have resulted from the loss of protection afforded by condoms and vaginal preparations used for contraception when the intrauterine device (IUD) and pill were used increasingly as the means of contraception.[14] This hypothesis is substantiated by the finding that there appears to be an inverse relation between the gonorrhea rates in Sweden and the use of condoms as indicated by statistics of imports of condoms into Sweden.[15] The demonstration, through studies *in vitro* and in the rabbit, of germicidal effects against *Treponema pallidum, Neisseria gonorrhea, Trichomonas vaginalis,* and *Candida albicans* of vaginal contraceptives now being marketed lend further support to this hypothesis.[16]

In discussions of prophylaxis or contraception by condom or vaginal preparation, comments frequently are made that "there is a high failure rate," "people won't use it all the time," or "it's too much of a hassle." There appears to be both professional and public antipathy toward, or lack of confidence in, the condom. It is necessary, however, to approach the matter from the public-health point of view and recognize that the control of any disease depends upon the full utilization of all available resources and methods to deal with the disease. Major advances have been made in the control of communicable disease such as malaria and tuberculosis in

the absence of highly specific therapeutic or vector-control agents. When it is possible, for instance, to legislate or mandate action, as in the fluoridation of water or the vitamin and mineral enrichment of flour or milk, a high degree of communitywide protection is obtained without need for involvement or cooperation by the patient. On the other hand, when individual motivation and cooperation are essential, as in immunization, failure to achieve the full possible reduction in disease incidence can be shown to be due, in varying measure, to uncooperative individual behavior, even though highly effective medical technology exists.

In considering venereal diseases, in particular syphilis, it is appropriate to recall that great success in the reduction of rates of complications and death were achieved in the United States before penicillin was discovered or was available for large-scale use. The success came about through a well-planned and highly cooperative national effort in which existing resources, including prophylaxis, were all used in a well-planned and coordinated national program. It consisted of effective professional and public educational programs, highly innovative programs of mass screening, and the introduction and development—to a high degree of effectiveness—of the interview of patients for identification of contacts and subsequent search for and treatment of the contacts.

It is important to reflect on some of the epidemiologic factors involved in the reduction of the reservoir of infectious diseases and consequent risk of spread. First, the risk of transmission of gonorrhea and syphilis is uncertain and variable; few well-controlled studies are available. However, in studies performed with human volunteers, even direct swabbing of pus taken from an acute male case of gonorrheal urethritis onto the everted meatus of the volunteer produced only 50% infection.[17] Epidemiologic studies reported by Holmes et al.[18] and others on the male show rates of risk ranging from 5 to 22%. In epidemiologic theory there is more than one means to reduce the incidence of a communicable disease: one is to reduce the reservoir of infection and, thus, the risk of exposure to a case; another is to raise the level of immunity of the person exposed or at risk, or to interpose barriers to the passage of the pathogens. Theoretical models with respect to the potential of a prophylactic preparation of varying levels of effectiveness and of usage in reducing the prevalence of gonorrhea have been developed by T.Y. Lee et al.[19] At the rates of increase which existed in the United States at the time of the study, in a population of 1,000 cases at the end of four years, 1,860 cases would be expected. The use of a

preparation which is only 50% effective as a prophylactic by 20% of the population at risk at each act of coitus theoretically could reduce the number of cases to seven at the end of the fourth year. Although this is theoretical, the military experience reported by Moore[6] showing one infection per 37 exposures without prophylaxis and one per 274 with prophylaxis suggest the validity of the model.

In view of the demonstrated contribution of prophylaxis as an element of effective VD control programs as well as of the theoretical projections, the steady rise in and the present high rates of gonorrhea and syphilis would seem to call for a reappraisal of the problem and the possibilities which prophylactic measures, adapted to current social and cultural climates, might offer in improving present programs. There is reason for hope, now that there seems to be a broadening of concern with the gamut of sexually transmissible diseases rather than the venereal diseases alone. The potential level in increase of interest among patients and professional persons resulting from this broader concept is self-evident. The new approach may be summarized in the report of Technical Discussions at the 28th World Health Assembly meeting in Geneva, May 23, 1975,[20] from which the following quotation is taken;

> In view of the increasing incidence of sexually transmitted diseases (which include not only syphilis, gonorrhea, and the other "venereal" diseases, but also a host of other diseases such as non-specific urethritis, genital herpes and trichomoniasis) and their considerable associated morbidity and resulting economic burden, a greater realization of their importance is required. As a consequence of emotional conflicts and behavioral changes generated by failures to adapt to changing societies, new groups at high risk for sexually transmitted diseases are emerging throughout the world. Many interrelated factors are responsible, including industrialization, urbanization, population mobility (secondary to work opportunities, increased availability of transport and increased tourism), and the social equality being accorded to women. Further delineation of these high risk groups is required so that outreach programs (including health education and screening) can be designed to meet their specific needs. It was noted that one high risk group of particular importance constituted patients presenting with sexually transmitted diseases to health care providers, and their sexual partners. Health authorities should review the extent of the prob-

lem in sexually transmitted diseases and the possibilities for their control, if necessary, so they may be afforded priority in budgetary allocations.

In the same document it was suggested that research was needed for "...acceptable and inexpensive prophylactic methods other than the condom (e.g., vaginal preparations and intra-uterine coils....)."

If it is possible to consider the venereal diseases in this broader context of health and to bring about widespread understanding of the obvious advantages of increased professional attention on the part of the personnel of venereal disease and family-planning programs, the potential for improved protection of patients and their coital partners through case-finding and prophylactic and contraceptive practices then should result in a reduction of both sexually transmitted diseases and unplanned pregnancy. The value of screening family-planning patients for gonorrhea is recognized in the policy statement of the U.S. Department of Health, Education, and Welfare calling for this procedure in federally funded family-planning programs. Experience shows that the rates of case-finding in this group (self-identified, at risk, seeking contraceptive services) parallel those in the communities from which the patients come.

Only recently has there been a reawakening of appreciation of the value and effectiveness of the condom and of vaginal preparations in contraception. A summarization appears in recent publications of the Department of Medical and Public Affairs of the George Washington University Medical Center.[4] The failure rates are variable with all vaginal preparations and the condom, but when used properly, their rates are in the same range as with the IUD and the pill. In analyses of the success and failure of the various methods, the human element is the critical factor, highlighting the importance of education, motivation, and self-discipline in addition to the ease of access to the methods.

In view of the potential for prevention of both unplanned pregnancy and venereal disease, clinical trials with several agents are now in progress[21] to develop vaginal contraceptive preparations which will be as effective as prophylactic agents as the condom is already. With vaginal preparations as well as the condom available over the counter, through vending machines, or through other marketing or distribution channels, the means for protection against pregnancy are accessible easily to the group at highest risk of unplanned pregnancy, a group which usually is not in contact with physicians who would prescribe the IUD or pill and is highly active sexually, as

shown by the high VD rate in the 15-to-24 year age group. Thus, the risk of pregnancy in this group is obvious since the pattern of sexual contact is shown by the high VD rate. Protection against VD through use of the condom by this group is obviously desirable and possible, as shown by the French experience reported by Siboulet,[22] in spite of the problems of motivation so well stated by Darrow.[2] The experience of Siboulet, in which 302 males 16 to 22 years of age who had contact with infected females but used condoms had only two cases of gonorrhea, in contrast to 465 cases in 480 males of the same ages whose partners had gonorrhea but who had not used condoms, clearly demonstrates the prophylactic value of the condom. The problem that remains is that of promoting more widespread use of the condom. If vaginal contraceptives are shown to be effective as prophylacatic agents, another tool will be added for use in efforts to control venereal disease.

It must be noted, however, that it appears to be necessary to develop new motivational approaches to assure the use of preparations and devices which are now freely available to the group at risk of unplanned pregnancy and sexually transmitted diseases. The literature is replete with studies showing knowledge of contraception techniques but lack of protective practice. A similar dichotomy between knowledge and practice is shown with respect to venereal disease. The consequent need to develop methods to motivate the high-risk group to practice self-protective behavior is evident and seems to merit high priority for study.

The most recent studies on the economic costs of VD[23] suggest clearly the need for development of additional and, perhaps, more acceptable methods for controlling sexually transmitted diseases, as well as for better use of existing methods. Past experience indicates vividly the need to reintroduce and modify, as appropriate to the group at high risk in today's society, the concepts of practice of prophylaxis. A move in this direction should be possible within present medical and public health technology and knowledge, by improving and updating methods for the motivation of individuals and groups to practice self-protection. It may well be, in terms of gonorrhea and syphilis, that not until the high-risk segment of the population becomes aware of the damage done by VD and perceives an individual risk that it will be possible to motivate this group to practice self-protection by prophylaxis.

As a public health worker who has seen the ability of the health professions to promote and assist in the integration of prophylactic con-

cepts and practices, I should prefer to see us take the leadership—developing improved methods as well as learning how to reach and motivate the group at risk to use current methods such as the condom, while setting the stage for new developments—rather than letting nature take her course, a toll in disease, disability, and even death.

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